(c) an amino acid sequence with at least one hydrophobic moiety substituted for the N-terminal amino acid,

wherein the protein, in the absence of the hydrophobic moiety, binds to a receptor or coreceptor, and the hydrophobic moiety does not substantially affect binding affinity of the protein to the receptor or coreceptor.

2. (**Reiterated**) The protein of claim 1, wherein the hydrophobic moiety is a peptide comprising at least one hydrophobic amino acid.

3. (**Reiterated**) The protein of claim 1, wherein the hydrophobic moiety is a lipid.

4. (**Reiterated**) The protein of claim 1, wherein the protein further comprises a hydrophobic moiety substituted for, or appended to, the C-terminal amino acid.

5. (**Reiterated**) The protein of claim 1, wherein the protein is an extracellular signaling protein.

6. (**Reiterated**) The protein of claim 1, wherein the N-terminal amino acid is a functional derivative of a cysteine.

7. (**Reiterated**) The protein of claim 1, wherein the protein is modified at both the N-terminal amino acid and the C-terminal amino acid.

8. (**Reiterated**) The protein of claims 4 or 7, wherein the protein has a hydrophobic moiety substituted for, or appended to, at least one internal amino acid.

9. (**Reiterated**) The protein of claim 1, wherein the protein has a hydrophobic moiety substituted for, or appended to, at least one amino acid intermediate to the N-terminal and C-terminal amino acids.

10. (**Reiterated**) The protein of claim 3, wherein the lipid moiety is a fatty acid selected from saturated and unsaturated fatty acids having between 2 and 24 carbon atoms.

14. (**Reiterated**) The protein of claim 1, further comprising a vesicle in contact with the hydrophobic moiety.

15. (**Reiterated**) The protein of claim 14, wherein the vesicle is selected from a cell membrane, a micelle, and a liposome.

28. (**Reiterated**) An isolated protein having a C-terminal amino acid and an N-terminal thioproline group, said group formed by reacting an aldehyde with an N-terminal cysteine of the protein, wherein the protein, in the absence of the thioproline group, binds to a receptor or coreceptor, and the thioproline group does not substantially affect binding affinity of the protein to the receptor or coreceptor.

29. (**Reiterated**) An isolated protein having a C-terminal amino acid and an N-terminal amide group, said group formed by reacting a fatty acid thioester with an N-terminal cysteine of the protein, wherein the protein, in the absence of the amide group, binds to a receptor or coreceptor, and the amide group does not substantially affect binding affinity of the protein to the receptor or coreceptor.

30. (**Reiterated**) An isolated protein having a C-terminal amino acid and an N-terminal maleimide group, said N-terminal maleimide group formed by reacting a maleimide group with the N-terminal cysteine of the protein, wherein the protein, in the absence of the maleimide group, binds to a receptor or coreceptor, and the maleimide group does not substantially affect binding affinity of the protein to the receptor or coreceptor.

31. (**Reiterated**) The isolated protein of claims 28, 29 or 30, wherein the C-terminal amino acid of the protein is modified with a hydrophobic moiety.

40. (**Reiterated**) A method for modifying a physico-chemical property of a protein, comprising introducing at least one hydrophobic moiety to an N-terminal cysteine of the protein or to a functional equivalent of the N-terminal cysteine, wherein the protein, in the absence of the hydrophobic moiety, binds to a receptor or coreceptor, and the hydrophobic moiety does not substantially affect binding affinity of the protein to the receptor or coreceptor.

41. (**Reiterated**) The method of claim 40, further comprising contacting the hydrophobic moiety with a vesicle.

42. (**Reiterated**) The method of claim 40, wherein the hydrophobic moiety is either a lipid moiety selected from saturated and an unsaturated fatty acids having between 2 and 24 carbon atoms or is a hydrophobic protein.

46. (**Reiterated**) The method of claim 41, wherein the step of contacting comprises contacting with a vesicle selected from a cell membrane, liposome and micelle.

48. (**Reiterated**) A modified protein, produced by the method of claim 40.

50. (**Reiterated**) A method for modifying a protein having a biological activity and containing an N-terminal cysteine, comprising reacting the N-terminal cysteine with a fatty acid thioester to form an amide, wherein such modification enhances the protein's biological activity, wherein the protein, in the absence of the modification, binds to a receptor or coreceptor, and the modification does not substantially affect binding affinity of the protein to the receptor or coreceptor.

53. (**Reiterated**) A method for modifying a protein having a biological activity and containing an N-terminal cysteine, comprising reacting the N-terminal cysteine with a maleimide group, wherein the protein, in the absence of the maleimide group, binds to a receptor or coreceptor, and the maleimide group does not substantially affect binding affinity of the protein to the receptor or coreceptor, and wherein such modification enhances the protein's biological activity.

56. (**Reiterated**) A method for modifying a protein that binds to an extracellular receptor, comprising appending a hydrophobic peptide to the protein, wherein the protein has a biological activity and the hydrophobic peptide enhances the biological activity.

57. (**Reiterated**) The method of claim 56, wherein the hydrophobic peptide is appended to an amino acid of the protein selected from the N-terminal amino acid, the C-terminal amino acid,

an amino acid intermediate between the N-terminal amino acid, and the C-terminal amino acid, and combinations of the foregoing.

63. (**Reiterated**) The method of claim 57, wherein the step of appending comprises replacing at least the N- terminal amino acid of the protein with at least one hydrophobic amino acid.

64. (**Reiterated**) The method of claim 63, wherein the at least one hydrophobic amino acid is a plurality of isoleucine residues.

65. (**Reiterated**) The method of claim 63, further comprising chemically modifying at least one of the isoleucine residues.

66. (**Reiterated**) An isolated protein having a C-terminal amino acid and an N-terminal acetamide group, said group formed by reacting a substituted acetamide with an N-terminal cysteine of the protein, wherein the protein, in the absence of the acetamide group, binds to a receptor or coreceptor, and the hydrophobic moiety does not substantially affect binding affinity of the protein to the receptor or coreceptor.

67. (**Reiterated**) An isolated protein having a C-terminal amino acid and an N-terminal thiomorpholine group, said group formed by reacting a haloketone group with an N-terminal cysteine of the protein, wherein the protein, in the absence of the thiomorpholine group, binds to a receptor or coreceptor, and the thiomorpholine group does not substantially affect binding affinity of the protein to the receptor or coreceptor.

68. (**Twice Amended**) A method for modifying a protein that binds to an extracellular domain of a cell membrane-associated receptor and contains an N-terminal cysteine, comprising reacting the N-terminal cysteine with a substituted acetamide group, wherein such modification enhances the protein's biological activity, wherein the protein has a biological activity, and the acetamide group enhances the biological activity of the protein.

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71. (**Reiterated**) A method for modifying a protein having a biological activity and containing an N-terminal cysteine, comprising reacting the N-terminal cysteine with a

haloketone group, wherein such modification enhances the protein's biological activity, wherein the protein, in the absence of the haloketone group, binds to a receptor or coreceptor, and the haloketone group does not substantially affect binding affinity of the protein to the receptor or coreceptor.

87. (**Amended**) A method for modifying a protein that binds an extracellular domain of a cell membrane-associated receptor, comprising treating the protein with an active thioester under conditions sufficient to acylate the protein, wherein the protein has a biological activity, and acylation of the protein enhances the biological activity of the protein.

88. (**Reiterated**) The method of claim 87, wherein the protein is acylated at an amino acid selected from the N-terminal amino acid, the C-terminal amino acid, an amino acid intermediate between the N-terminal amino acid and the C-terminal amino acid, and combinations of the foregoing.

89. (**Amended**) A method for modifying a protein that binds an extracellular domain of a cell membrane-associated receptor and contains an N-terminal cysteine, comprising reacting the N-terminal cysteine with a fatty acid active thioester to form an amide, wherein the protein has a biological activity, and the modification enhances the biological activity of the protein.

93. (**Amended**) An isolated polypeptide ligand for a receptor, which receptor includes an extracellular domain and which receptor is membrane-associated, wherein the ligand is covalently attached to a hydrophobic moiety that enhances the biological activity of the ligand relative to the biological activity of the ligand in the absence of the hydrophobic moiety.

94. (**Amended**) The ligand of claim 93, wherein the hydrophobic moiety is a peptide comprising at least one hydrophobic amino acid.

95. (**Amended**) The ligand of claim 93, wherein the hydrophobic moiety is a lipid.

96. (**Amended**) The ligand of claim 93, wherein the protein further comprises a hydrophobic moiety substituted for, or appended to, the C-terminal amino acid.

97. (**Amended**) The ligand of claim 93, wherein the protein is an extracellular signaling protein.

98. (**Amended**) The ligand of claim 93, wherein the N-terminal amino acid is a functional derivative of a cysteine.

99. (**Amended**) The ligand of claim 93, wherein the ligand is modified at both the N-terminal amino acid and the C-terminal amino acid.

100. (**Amended**) The ligand of claim 96 or 99, wherein the ligand has a hydrophobic moiety substituted for, or appended to, at least one internal amino acid.

101. (**Amended**) The ligand of claim 93, wherein the ligand has a hydrophobic moiety substituted for, or appended to, at least one amino acid intermediate to the N-terminal and C-terminal amino acids.

102. (**Amended**) The ligand of claim 95, wherein the lipid moiety is a fatty acid selected from saturated and unsaturated fatty acids having between 2 and 24 carbon atoms.

103. (**Amended**) The ligand of claim 93, further comprising a vesicle in contact with the hydrophobic moiety.

104. (**Amended**) The ligand of claim 103, wherein the vesicle is selected from a cell membrane, a micelle, and a liposome.

The claims presented above incorporate changes as indicated by the marked-up versions below.

1. (**Twice Amended**) An isolated protein comprising an N-terminal amino acid and a C-terminal amino acid, wherein the protein comprises an amino acid sequence ~~is~~ selected from:

(a) ~~a protein~~ an amino acid sequence with an N-terminal cysteine that is appended with at least one hydrophobic moiety;

(b) ~~a protein~~ an amino acid sequence with an N-terminal amino acid that is not a cysteine appended with at least one hydrophobic moiety; and

(c) ~~a protein~~ an amino acid sequence with at least one hydrophobic moiety substituted for the N-terminal amino acid,

wherein the protein, in the absence of the hydrophobic moiety, binds to a receptor or coreceptor, and the hydrophobic moiety does not substantially affect binding affinity of the protein to the receptor or coreceptor.

68. (**Twice Amended**) A method for modifying a protein that binds to an extracellular domain of a cell membrane-associated receptor and contains an N-terminal cysteine, comprising reacting the N-terminal cysteine with a substituted acetamide group, wherein such modification enhances the protein's biological activity, wherein the protein has a biological activity, and the acetamide group enhances the biological activity of the protein.

87. (**Amended**) A method for modifying a protein that binds an extracellular domain of a cell membrane-associated receptor, comprising treating the protein with an active thioester under conditions sufficient to acylate the protein, wherein the protein has a biological activity, and acylation of the protein ~~the hydrophobic moiety~~ enhances the biological activity of the protein.

89. (**Amended**) A method for modifying a protein that binds an extracellular domain of a cell membrane-associated receptor and contains an N-terminal cysteine, comprising reacting the N-terminal cysteine with a fatty acid active thioester to form an amide, wherein the protein has a biological activity, and the modification enhances the biological activity of the protein.

93. (**Amended**) An isolated polypeptide ligand for ~~an extracellular~~ a receptor, which receptor includes an extracellular domain and which receptor is membrane-associated, wherein the ligand is covalently attached to a hydrophobic moiety that enhances the biological activity of the ligand relative to the biological activity of the ligand in the absence of the hydrophobic moiety.

94. (**Amended**) The ~~protein~~ ligand of claim 93, wherein the hydrophobic moiety is a peptide comprising at least one hydrophobic amino acid.

95. (**Amended**) The ~~protein~~ ligand of claim 93, wherein the hydrophobic moiety is a lipid.

96. (**Amended**) The ~~protein~~ ligand of claim 93, wherein the protein further comprises a hydrophobic moiety substituted for, or appended to, the C-terminal amino acid.

97. (**Amended**) The ~~protein~~ ligand of claim 93, wherein the protein is an extracellular signaling protein.

98. (**Amended**) The ~~protein~~ ligand of claim 93, wherein the N-terminal amino acid is a functional derivative of a cysteine.

99. (**Amended**) The ~~protein~~ ligand of claim 93, wherein the ~~protein~~ ligand is modified at both the N-terminal amino acid and the C-terminal amino acid.

100. (**Amended**) The ~~protein~~ ligand of claim 96 or 99, wherein the ~~protein~~ ligand has a hydrophobic moiety substituted for, or appended to, at least one internal amino acid.

101. (**Amended**) The ~~protein~~ ligand of claim 93, wherein the ~~protein~~ ligand has a hydrophobic moiety substituted for, or appended to, at least one amino acid intermediate to the N-terminal and C-terminal amino acids.

102. (**Amended**) The ~~protein~~ ligand of claim 95, wherein the lipid moiety is a fatty acid selected from saturated and unsaturated fatty acids having between 2 and 24 carbon atoms.

103. (**Amended**) The ~~protein~~ ligand of claim 93, further comprising a vesicle in contact with the hydrophobic moiety.

104. (**Amended**) The ~~protein~~ ligand of claim 103, wherein the vesicle is selected from a cell membrane, a micelle, and a liposome.